# Guidance for Industry and Review Staff

## Labeling for Human Prescription Drugs — Determining Established Pharmacologic Class for Use in the Highlights of Prescribing Information

Good Review Practice

***DRAFT GUIDANCE***

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For questions regarding this draft document contact William Pierce at 301-796-0900.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**

**May 2007**
**Labeling**

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**U.S. Department of Health and Human Services**
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# Guidance for Industry and Review Staff[1] Labeling for Human Prescription Drugs — Determining Established Pharmacologic Class for Use in the Highlights of Prescribing Information

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## I. INTRODUCTION

This guidance is intended to help applicants and the review staff in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA) determine when a drug[2] belongs to an established pharmacologic class as well as how to select the appropriate word or phrase (term) that describes the pharmacologic class for inclusion in the *Indications and Usage* section of Highlights of Prescribing Information (*Highlights*) of approved labeling.

Although not specifically required, the pharmacologic class can also appear in other sections of labeling. This guidance applies to the use of the pharmacologic class in the *Indications and Usage* section of *Highlights* only.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required. Although guidance

[1] This guidance has been prepared by the Office of New Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

[2] For the purposes of this guidance, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

documents do not legally bind FDA, review staff may depart from guidance documents only with appropriate justification and supervisory concurrence.

## II. BACKGROUND

In January 2006, the FDA published a final rule that amended the requirements for the content and format of labeling for human prescription drug and biological products.[3] The new labeling format is intended to make it easier for health care professionals to access, read, and use the information in prescription drug labeling, thereby facilitating professionals' use of labeling to make prescribing decisions.

The rule requires the following statement to appear under the *Indications and Usage* section of *Highlights* if a drug is a member of an established pharmacologic class:[4]

> "(Drug) is a (name of class) indicated for (indication(s))."

If a drug does ***not*** have an ***established*** pharmacologic class, the statement must be omitted from the *Indications and Usage* section of *Highlights*.

Knowing the established pharmacologic class can provide health care professionals with important information about what to expect from a drug and how it relates to other therapeutic options. Such information can also help reduce the risk of duplicative therapy and drug interactions.

## III. DEFINITIONS

### A. Pharmacologic Class

For purposes of this guidance, a *pharmacologic class* is a group of drug or biological products that share scientifically documented properties related to safety and effectiveness. Specifically, for purposes of this guidance, *pharmacologic class* is defined on the basis of any one of the following three attributes of the drug substance:

1. Mechanism of action (MOA) — Pharmacologic action at the receptor, membrane, or tissue level

2. Physiologic effect (PE) — Pharmacologic effect at the organ, system, or whole body level

3. Chemical structure (CS)

[3] See 21 CFR parts 201, 314, and 601 *Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products* (71 FR 3922).

[4] See 21 CFR 201.57(a)(6).

### B. *Established* Pharmacologic Class

An ***established*** pharmacologic class is one that the FDA has determined to be scientifically valid ***and*** clinically meaningful according to the following definitions:

- A *scientifically valid* pharmacologic class is supported by documented and submitted empiric evidence showing that the drug's pharmacologic class is known, not theoretical, and relevant and specific to the indication.

- A *clinically meaningful* pharmacologic class enhances the ability of professionals to understand therapeutic effects related to the indication or to anticipate undesirable effects that may be associated with the drug.

## IV. IDENTIFYING AN ESTABLISHED PHARMACOLOGIC CLASS

It is often possible to identify multiple scientifically valid pharmacologic classes. However, only pharmacologic classes that are also ***clinically meaningful*** will be considered to be established pharmacologic classes. Consider the following examples:

- Drug A
  MOA = Beta-adrenergic blocker
  PE = Negative inotropy and chronotropy
  CS = Benzeneacetamide

  In this case, the most clinically meaningful term is the MOA.

  "Drug A is a ***beta-adrenergic blocker*** indicated for treatment of hypertension."

- Drug B
  MOA = Inhibitor of reabsorption of sodium and chloride ions in the kidney
  PE = Loop diuretic
  CS = Anthranilic acid derivative

  In this case, the most clinically meaningful term is the PE.

  "Drug B is a ***loop diuretic*** indicated for treatment of edema associated with congestive heart failure."

- Drug C
  MOA = GABA A and B Modulator
  PE = Increased GABA activity
  CS = Benzodiazepine

In this case, the most clinically meaningful term is the CS.

"Drug C is a ***benzodiazepine*** indicated for management of anxiety disorders."

It may be appropriate to include a combination of established pharmacologic classes if more than one attribute of the drug is clinically meaningful. The following situations are examples of when it is appropriate to use multiple established pharmacologic classes:

- The CS provides additional meaningful information to prescribers beyond that provided by MOA or PE alone.

  "Drug D is a ***thiazide diuretic*** indicated for treatment of edema associated with congestive heart failure."

- A combination of different levels of specificity of MOA or PE provides clinically meaningful information to prescribers.

Many drugs contain more than one active ingredient. These active ingredients can be members of the same or different pharmacologic classes. These pharmacologic classes can apply to the same or different indications. The following examples illustrate different situations that may be encountered:

- For products with more than one drug where all drugs are in the same pharmacologic class:

  "Product X is a combination of Drug E and Drug F, both ***HIV nucleoside analog reverse transcriptase inhibitors***, indicated for use in combination with other antiretroviral agents for treatment of HIV infection."

- For products with more than one drug where the drugs are from different pharmacologic classes:

  "Product Y is a combination of Drug G, a ***thiazide diuretic***, and Drug H, a ***potassium-sparing diuretic***, indicated for hypertension."

  Note: For drugs that are not combination products but are approved for use with other drug products named specifically by proprietary name or nonproprietary name in the *Indications and Usage* section, the pharmacologic class for the concomitant drug should not be included.

## V. IDENTIFYING THE MOST APPROPRIATE TERM TO DESCRIBE AN ESTABLISHED PHARMACOLOGIC CLASS

For new drugs that are undergoing review for marketing or licensing approval, the FDA will review a proposed established pharmacologic class for scientific validity based on

submitted evidence supporting the claim that the pharmacologic class is known and relevant to the indication under review. The FDA will also evaluate the clinical meaningfulness of the proposed class based on the potential for this classification to aid in the understanding of the drug's effects, including side effects.

According to 21 CFR 314.70(b)(2)(v)(C), for approved drugs for which the applicant plans to update the labeling or convert the labeling to a format consistent with the final rule, the addition of an established pharmacologic class term to the *Indications and Usage* section of *Highlights* of approved drug labeling is a change that must be proposed and submitted in a prior-approval labeling supplement.

When identifying a term to describe an established pharmacologic class for a drug, it is important to consider other drugs that share therapeutic, mechanistic, or structural similarity. Misleading or potentially confusing established pharmacologic class terms can be avoided by achieving consistency in terminology, where appropriate, across drugs used for similar purposes.

Along with the proprietary name, the drug product's established name (or the proper name or names for a biological product) must be displayed at the beginning of *Highlights*.[5] If the established name or proper name that is displayed at the beginning of *Highlights* includes a term that may also serve as an established pharmacologic class, that term should not be included under the *Indications and Usage* section of *Highlights*.

Parentheses should not be used to indicate auxiliary or less-important pharmacologic class terms.

[5] See 21 CFR 201.57(a)(2).